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### **Manganese Complexes in Brain Mitochondria**

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Beamline(s): X9B

**Introduction:** Manganese inhaled from dust primarily affects the basal ganglia and induces symptoms in welders, metal workers, and miners somewhat similar to those of Parkinsonism. MMT, a manganese compound, is currently being used as a gasoline additive in the US and Canada, exposing vast populations to Mn-containing dust. Inside neuronal tissue, manganese is sequestered by mitochondria. The oxidation state of intraneuronal and intramitochondrial manganese is an important factor in hypotheses concerning the mechanism by which manganese acts.

During the period 10/01/00 to 9/30/01, we used the facilities of beamline X9B at the National Synchrotron Light source at Brookhaven National Laboratory to study manganese in brain mitochondria and have begun studies of manganese in neuron-like cells. The primary goal was to determine the amounts of  $Mn^{2+}$  and  $Mn^{3+}$  present under a range of relevant conditions in brain mitochondria and cells. A secondary goal was to determine the manganese complexes present in these samples.

**Methods and Materials:** Manganese in frozen mitochondrial samples and cell samples.

**Results:** Results have shown that at very low levels of mitochondrial manganese (endogenous manganese at around 0.075 nmoles Mn/mg protein),  $Mn^{2+}$  is present and there is inconclusive evidence for a small amount of  $Mn^{3+}$ . This is probably held in mitochondrial superoxide dismutase. Even though mitochondria are the source of the highest production of superoxide radical and superoxide is known to oxidize  $Mn^{2+}$  to  $Mn^{3+}$ , and even though we tested protocols, which should have exposed the samples to significant superoxide, there was no evidence for any accumulation of  $Mn^{3+}$  above that found endogenously even where significantly more manganese was present in the mitochondria. This must mean that even though  $Mn^{3+}$  could be produced by the conditions used, it was not stabilized inside the mitochondria. The shape of the XANES spectra of intramitochondrial manganese was essentially identical in liver, heart, and brain mitochondria, demonstrating that there are no significant amounts of any special manganese complexes formed in brain mitochondria. The XANES spectra suggested that intramitochondrial manganese above that found endogenously is primarily in (+2) complexes with ATP and biphosphate.

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